UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,938	07/10/2001	Michael Econs	053884-5001	9281

23973 7590 03/06/2006

DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
SAOUD, CHRISTINE J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,938	ECONS ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35 and 39-83* is/are pending in the application.

4a) Of the above claim(s) *17-31,34,35,39-42 and 44-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16, 32-33 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: alignment.

DETAILED ACTION

Response to Amendment

Claims 1-4 and 43 have been amended as requested in the reply filed 02 December 2005. Claims 1-35 and 39-83 are pending in the instant application. Claims 17-31, 34-35, 39-42, 44-83 remain withdrawn as being drawn to a nonelected invention, said election made without traverse in Paper No. 8, filed 04 April 2003. Claims 1-16, 32-33 and 43 are currently under examination in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 02 December 2005 have been fully considered but they are not deemed to be persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 32 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:1 (or 98% or 99% identity to SEQ ID NO:1) encoding a polypeptide which has the ability to bind an FGF receptor and increase phosphate transport, does not reasonably provide enablement for a nucleic acid molecule which encodes a polypeptide that can "alter phosphate transport". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims encompass nucleic acid molecules having some degree of sequence identity to SEQ ID NO:1, wherein the nucleic acid molecules encode a polypeptide that "has the ability to bind an FGF receptor and alter phosphate transport". The recitation of "alter phosphate transport" implies that the polypeptides encoded by the nucleic acids of the claims would be able to both increase and decrease phosphate transport by binding to an FGF receptor. However, the instant specification has not enabled the full scope of the instant claims because no molecules which bind an FGF receptor and decrease phosphate transport have been made or disclosed. The FGF23 polypeptide of the instant application is a protein that regulates phosphate metabolism. The full length protein facilitates the transport of phosphate. The full length protein contains a cleavage site in the general area of amino acids 176 and 179, and upon cleavage with an enzyme, the FGF23 protein is no longer able to regulate phosphate transport. Mutant proteins have been discovered in which the cleavage site of the

FGF23 protein is altered and cleavage cannot occur, resulting in FGF23 molecules which cause phosphate transport and cannot be turned off by the body, resulting in hypophosphate disorders.

There is no disclosure of molecules of FGF23 which bind an FGF receptor and decrease phosphate transport. There is no teaching in the instant specification as to which amino acids are involved in receptor binding and receptor activation such that the skilled artisan could design a molecule which bound the receptor and either decreased phosphate transport or which inhibited phosphate transport. It is clear that the instant specification has taught a nucleic acid molecule of SEQ ID NO:1 which encodes a protein of SEQ ID NO:2. It is clear that the instant specification has taught natural mutants of FGF23 which inhibit cleavage of the full-length protein. However, the instant specification has not taught the full breadth of what is currently claimed, namely polypeptides which have the ability to bind an FGF receptor and "alter" phosphate transport. The skill in the art is high, but the unpredictability in the art is also high. The lack of disclosure of receptor binding regions of the polypeptide, lack of disclosure of receptor activation regions of the polypeptide, the lack of working examples, the lack of knowledge in the prior art for similar molecules, and the need for significant experimentation leads one to the conclusion that the experimentation required to practice the full breadth of the claims is undue, and the claims are not enabled for their entire breadth.

Applicant may wish to amend the claims to reflect the activity of increasing phosphate transport, which would avoid this ground of rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16, 32-33 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims include language such as "encoding a fibroblast growth factor-23" and "a nucleic acid having the sequence of at least one of SEQ ID NO:1". These recitations imply that there are more than one molecule being referenced, such as more than one FGF-23 and more than one sequence of SEQ ID NO:1. Claims 1-3 and 12 refer to "encoding a fibroblast growth factor-23" and claim 4 is directed to an "isolated FGF23 nucleic acid". As pointed out previously, the mere recitation of "fibroblast growth factor-23" fails to convey any particular structure or protein because the art acknowledges that many proteins may go by different names as well as some names which can signify many different proteins. Therefore, because the recitation of a name places no material limitations on what is being claimed, it is not clear what is intended by the recitation, making the claims indefinite. Further, the DSMZ deposit may contain more than one nucleic acid molecule, based on the language that the claimed nucleic acid is "included" in the Deposit. Because "FGF23 nucleic acid" has no accepted meaning in the art, it is unclear what nucleic acid in the Deposit is encompassed by the claims.

Similarly, claim 1 is directed to an isolated nucleic acid comprising the nucleic acid sequence of SEQ ID NO:1. The current language of the claim includes encoding language and activity language for the polypeptide. However, the nucleic acid molecule is not what conveys activity on the encoded polypeptide – rather, it is the expression of the polypeptide under appropriate conditions that results in a functional, active molecule. "An isolated nucleic acid comprising SEQ ID NO:1" would be definite, enabled and free of the prior art of record.

Claim 3 includes duplicative language of "encoding" with "a fibroblast growth factor-23" and "polypeptide". This claim could be simplified and made clear by eliminating some of the language to more particularly point out what is being claimed. For example: "An isolated nucleic acid encoding a polypeptide having the amino acid sequence of SEQ ID NO:2". or "An isolated nucleic acid encoding a polypeptide having 98% identity to SEQ ID NO:2, wherein the polypeptide has the ability to increase phosphate transport". These claims are definite, enabled and appear to be free of the prior art of record.

Claims 2 and 13 refer to "a nucleic acid having the sequence of at least one of SEQ ID NO:1". There is only one sequence present in SEQ ID NO:1, therefore, the inclusion of the recitation of "at least one of" is unclear and indefinite.

Claim 2 could be worded "An isolated nucleic acid having 99% sequence identity SEQ ID NO:1, wherein the nucleic acid encodes a polypeptide having the ability to increase phosphate transport". Claim 3 could be similarly worded.

Claim 12 is unclear and indefinite because there is a lack of punctuation between SEQ ID NO:1 and "encoding". The claim could be interpreted as the isolated nucleic acid encoding a fibroblast growth factor-23, or that SEQ ID NO:1 is the "encoding" sequence. Again on this claim, the recitation of "encoding a fibroblast growth factor-23" is not necessary and is also indefinite for the reasons provided above. See also rejection of claim below.

Claim 13 contains language which makes it unclear what is being claimed: "wherein said complementary nucleic acid shares at least 99% sequence identity with a nucleic acid complementary with a nucleic acid having the sequence of at least one of SEQ ID NO:1". It appears that Applicant would like to claim complementary molecules of SEQ ID NO:1. The current language of claim 12 has no size limitation, which opens the claim to art (see rejection below). Applicant could file claims as follows:

1. An isolated nucleic acid comprising SEQ ID NO:1, or its complement.
2. An isolated nucleic acid of claim 1, comprising SEQ ID NO:1.
3. An isolated nucleic acid of claim 1, comprising the complement of SEQ ID NO:1.
4. An isolated nucleic acid 99% identical to SEQ ID NO:1, wherein the nucleic acid encodes a polypeptide which has the ability to increase phosphate transport.
5. An isolated nucleic acid which is 99% identical to the complement of SEQ ID NO:1.

This is just suggested language which would avoid the rejections raised above.

Claim 5 is unclear and indefinite for the recitation of "encoding a tag polypeptide covalently linked thereto". The claim is directed to a nucleic acid molecule. The "covalently linked thereto" recitation appears to be directed to how the tag polypeptide would be attached to the encoded polypeptide of the original nucleic acid molecule. This recitation does not place any limitation on the nucleic acid molecule and does not further define the nucleic acid molecule. If the claim is intended to encode a fusion molecule (SEQ ID NO:1 + nucleic acid encoding a tag polypeptide), then the language of covalent attachment should be avoided. The tag polypeptide could be on either the N-terminal or C-terminal end of the encoded polypeptide, so orientation does not need to be specified.

Claim 9 is unclear and indefinite for the recitation "comprising a nucleic acid specifying a promoter/regulatory sequence operably linked thereto". A nucleic acid molecule does not "specify" sequences – it encodes for things or comprises a sequence. The language of currently pending claim 7 can be used as a guide.

Claim Rejections - 35 USC § 102

Applicant's arguments regarding the rejections over Itoh et al. and Milne-Edwards et al. are persuasive. These rejections have been withdrawn.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Mahairas et al. (Proc. Natl. Acad. Sci. U.S.A. 96(17): 9739-9744, 1999).

Claim 12 is directed to an isolated nucleic acid complementary to a nucleic acid comprising SEQ ID NO:1, and claim 13 requires the complementary molecule be at least 99% identity to SEQ ID NO:1. However, the claims do not require complementation over the entire length of SEQ ID NO:1. Therefore, after a fair reading of the claims, molecules which share complementary regions could be encompassed by the claims.

Mahairas et al. teach a nucleic acid molecule which shares 3 long stretches of nucleotides which are 100% complementary to SEQ ID NO:1. (See attached sequence alignment). Therefore, Mahairas et al. anticipates the instant claims.

This ground of rejection could be avoided by adopting the suggested language indicated in the above rejections.

Allowable Subject Matter

The instant application contains allowable subject matter, including the nucleic acid molecule of SEQ ID NO:1, a nucleic acid encoding a polypeptide having the amino acid sequence of SEQ ID NO:2, and a nucleic acid molecule of SEQ ID NO:1 having the specific point mutations listed in the specification. Suggested language has been provided which would avoid rejections of record. New grounds of rejection were made therefore, this Office action is not final. The delay in flushing out these issues is regrettable.

Applicant should be advised that there are currently claims pending to non-elected inventions. The instant application cannot be allowed until the non-elected claims have been canceled.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on mttr, 8:00-2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud

```
  TITLE     Use of BAC End Sequences from Library RPCI-11 for Sequence-Ready
            Map Building
  JOURNAL   Unpublished (1997)
COMMENT     Other_GSSs: RPCI-11-177D20.TV
            Contact: Shaying Zhao, William Nierman, Mark Adams
            Department of Eukaryotic Genomics
            The Institute for Genomic Research
            9712 Medical Center Dr., Rockville, MD 20850
            Tel: 301 838 0200
            Pax: 301 838 0208
            Email: hbe@tigr.org
            Clones are derived from the human BAC library RPCI-11. For BAC
            library availability, please contact Pieter de Jong
            (pieter@dejong.med.buffalo.edu). Clones may be purchased from
            BACPAC Resources (http://bacpac.med.buffalo.edu/ordering) or from
            Research Genet cs (info@resgen.com). BAC end search page:
            http://www.tigr.org/tdb/humgen/bac_end_search/bac_end_search.html.
            Seq primer: SP6
            Class: BAC ends.
FEATURES              Location/Qualifiers
     source           1. .438
                      /organism="Homo sapiens"
                      /db_xref="GDB:7567675"
                      /db_xref="taxon:9606"
                      /clone="RPCI-11-177D20"
                      /clone_lib="RPCI-11"
                      /sex="Male"
                      /cell_type="Lymphocytes"
                      /note="Vector: pBACe3.6; Site_1: EcoRI; Site_2: EcoRI;
                      RPCI11 Human Male BAC Library"
BASE COUNT      123 a     73 c    116 g    126 t
ORIGIN

  Query Match             6.4%;  Score 102.8;  DB 17;  Length 438;
  Best Local Similarity   79.2%;  Pred. No. 3.4e-08;
  Matches  122;  Conservative    0;  Mismatches   32;  Indels    0;  Gaps    0;

Qy     317 GAATGGCCATGTGGATGGCGCACCCCATCAGACCATCTACAGTGCCCTGATGATCAGATC 376
           | ||||| ||| | |    |   ||       | |    ||||||||||||||||||||
Db     213 GGATGGCAATGAGTCTTTGCCCTGCCTGTTTTTCTCCATATGTGCCCTGATGATCAGATC 272

Qy     377 AGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGATGAGCAGAAGATACCTCTGCATGGA 436
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     273 AGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGATGAGCAGAAGATACCTCTGCATGGA 332

Qy     437 TTTCAGAGGCAACATTTTTGGATCACACTATTTC 470
           ||||||| ||||||| |||||||||     ||||
Db     333 TTTCAGATGCAACATATTTGGATCATTGAGTTTC 366


RESULT 5
AQ570344
LOCUS       AQ570344                 564 bp    DNA     linear   GSS 01-JUN-1999
DEFINITION  HS_5352_B1_G09_T7A RPCI-11 Human Male BAC Library Homo sapiens
            genomic clone Plate=928 Col=17 Row=N, DNA sequence.
ACCESSION   AQ570344
VERSION     AQ570344.1  GI:4963564
KEYWORDS    GSS.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 564)
  AUTHORS   Mahairas,G.G., Wallace,J.C., Smith,K., Swartzell,S., Holzman,T.,
            Keller,A., Shaker,R., Furlong,J., Young,J., Zhao,S., Adams,M.D. and
            Hood,L.
  TITLE     Sequence-tagged connectors: A sequence approach to mapping and
            scanning the human genome
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 96 (17), 9739-9744 (1999)
  MEDLINE   99380589
COMMENT     Contact: Mahairas GG, Wallace JC, Hood L
            High Throughput Sequencing Center
            University of Washington
            401 Queen Anne Avenue North, Seattle, WA 98109, USA
            Tel: (206) 616-3618
            Pax: (206) 616-3887
            Email: jwallace@u.washington.edu
            Clones are derived from the human BAC library RPCI-11. For BAC
            library availability, please contact Pieter de Jong
            (pieter@dejong.med.buffalo.edu). Clones may be purchased from
            BACPAC Resources (http://bacpac.med.buffalo.edu/ordering_bac.htm)
            or from Resear h Genetics (info@resgen.com). BAC end Web Server:
            http://www.htsc.washington.edu
            Plate: 928  row: N  column: 17
            Seq primer: T7
            Class: BAC ends
            High quality sequence stop: 564.
FEATURES              Location/Qualifiers
     source           1. .564
                      /organism="Homo sapiens"
                      /db_xref="taxon:9606"
                      /clone="Plate=928 Col=17 Row=N"
                      /clone_lib="RPCI-11 Human Male BAC Library"
                      /sex="male"
                      /note="Vector: pBACe3.6; Site_1: EcoRI; Site_2: EcoRI;
                      Male blood DNA was isolated from one randomly chosen donor
                      and partially digested with a combination of EcoRI and
                      EcoRI Methylase. Size selected DNA was cloned into the
                      pBACe3.6 vector at EcoRI sites"
BASE COUNT      152 a    100 c    138 g    169 t      5 others
ORIGIN

  Query Match             6.2%;  Score 99.6;  DB 17;  Length 564;
  Best Local Similarity   77.9%;  Pred. No. 1.1e-07;
  Matches  120;  Conservative    0;  Mismatches   34;  Indels    0;  Gaps    0;

Qy     317 GAATGGCCATGTGGATGGCGCACCCCATCAGACCATCTACAGTGCCCTGATGATCAGATC 376
           | ||||| ||| | |    |   ||       | |    ||||||||||||||||||||
Db     244 GGATGGCAATGAGTCTTTGCCCTGCCTGTTTTTCTCCATAGGTGCCCTGATGATCAGATC 303

Qy     377 AGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGATGAGCAGAAGATACCTCTGCATGGA 436
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     304 ACAGGATGCTGGCTTTGTGGTGATTACACGTGTGATGAGCAGAAGATACCTCTGCATGGA 363

Qy     437 TTTCAGAGGCAACATTTTTGGATCACACTATTTC 470
           ||||||| ||||||||| |||||||     ||||
Db     364 TTTCAGATGCAACATTTGTGGATCAGTGAGTTTC 397


RESULT 6
BE869144
LOCUS       BE869144                 741 bp    mRNA    linear   EST 20-OCT-2000
DEFINITION  601445130F1 NIH_MGC_65 Homo sapiens cDNA clone IMAGE:3849343 5',
            mRNA sequence.
ACCESSION   BE869144
VERSION     BE869144.1  GI:10317920
KEYWORDS    EST.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 741)
  AUTHORS   NIH-MGC http://mgc.nci.nih.gov/.
  TITLE     National Institutes of Health, Mammalian Gene Collection (MGC)
  JOURNAL   Unpublished (1999)
COMMENT     Contact: Robert Strausberg, Ph.D.
            Email: cgapbs-r@mail.nih.gov
            Tissue Procurement: ATCC
            cDNA Library Preparation: Life Technologies, Inc.
            cDNA Library Arrayed by: The I.M.A.G.E. Consortium (LLNL)
            DNA Sequencing by: Incyte Genomics, Inc.
            Clone distribution: MGC clone distribution information can be
            found through the I.M.A.G.E. Consortium/LLNL at:
            http://image.llnl.gov
            Plate: LLAM9566  row: k  column: 08
            High quality sequence stop: 696.
```